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Effect of *Momordica charantia* Fruit Extract on Normal and Alloxan-Diabetic Rats

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Abstract: The antidiabetic activity of *Momordica charantia* (bitter gourd) fruit Methanol Extract (MCE) was investigated in normal and diabetic rats. Animals were treated intraperitoneally with a single dose of 120 mg kg⁻¹ alloxan to induce diabetes. This resulted in significant increase in plasma glucose level. The diabetic and normal rats were both randomly divided into 5 groups. Group A (control) received distilled water ad libitum. Groups B, C and D were treated orally with daily doses of 200, 400 and 600 mg kg⁻¹ of MCE respectively for 28 days. Group E received 10 mg kg⁻¹ chlorpropamide for the same period. Administration of MCE produced a dose-dependent decrease in blood glucose level in both normal and diabetic animals. The decrease was significant (p<0.05) with 400 and 600 mg kg⁻¹ of the extract. This is comparable to the effect of chlorpropamide. Contrary to some negative findings, the results of this study show that chronic oral administration of extract of *Momordica charantia* fruits at an appropriate dosage may be a good alternative antidiabetic agent.

Key words: Hypoglycemic, anti-diabetic, chlorpropamide, oxidative method, methanol, intraperitoneal

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder with impaired glucose tolerance and high risk of cardiovascular diseases (Schnell and Standl, 2006). The number of people with type I and type II diabetes are dramatically increasing worldwide (Pavana *et al.*, 2008). According to World Health Organization, about 170 million people are currently affected by diabetes and the figure is expected to double by the year 2025 (Boyle *et al.*, 2001). Diabetes mellitus is mainly due to relatively low level of insulin production or an inability of the body to use insulin properly which in turn leads to hyperglycemia (Virella-Lopes and Virella, 2003). Numerous experimental and clinical observations have indicated that hyperglycemia may directly or indirectly contribute to excessive formation of free radical which may result in many degenerative and inflammatory disorders (Ceriello, 2003). Diabetes is also known to involve oxidative stress and changes in lipid metabolism (Scoppola *et al.*, 2001). These changes are usually associated with microvascular and macrovascular complications which are the major causes of morbidity and mortality in diabetic individuals (El-Ghaffar and El-Said, 2006). Many oral and parenteral synthetic

antidiabetic agents have been developed to bring relief to sufferers of diabetes mellitus, but these drugs are either too expensive or possess undesirable side-effects and contra-indications (Adewole and Ojewole, 2008). Therefore, there is the need to search for more effective and safer hypoglycemic agents from plants and other natural sources (Krishna *et al.*, 2004). Medicinal plants constitute an important source of potential therapeutic agents for many diseases and there is a large volume of scientific data which support the anti-diabetic effects of many of these plants (Grover *et al.*, 2002). There are many reasons why medicinal plants should be subjected to scientific investigations. Foremost among these reasons is the recognizable therapeutic effects of many herbal remedies and the possibility that they may also have toxic side-effects (Keen *et al.*, 1994).

Momordica charantia L. commonly known as bittergourd is an economically important medicinal plant belonging to the family Cucurbitaceae. It is also known as bitter melon, balsam pear and Karela. In Nigeria and many other parts of the world, fruits and seeds of bittergourd have been used by traditional healers to treat ulcer, HIV, inflammation and cancer (Assubaie and El-Garawany, 2004). The plant is also famous for its traditional use in diabetes mellitus

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(Paul and Raychaudhuri, 2010; Karim *et al.*, 2011). Therefore this plant could be a good source of alternative treatment for diabetes mellitus.

The present study was undertaken to investigate the hypoglycemic properties of *Momordica charantia* fruit extract in rats.

MATERIALS AND METHODS

Plant material: Fresh fruits of *Momordica charantia* were collected in sufficient quantity from Ile-Ife, Nigeria. The study was carried out in the year 2010. The plant was authenticated by a Botanist of the Department of Botany, Obafemi Awolowo University, Ile-Ife, Nigeria. The fresh fruits were carefully washed with tap water to remove dust and other foreign materials. They were then air-dried in the laboratory. The dry fruits were blended into a powdery form using mortar and pestle. The 10 g of the powdered fruit was weighed and extracted in methanol at 52°C to obtain solid sample. The Methanol Extract (MCE) was stored at 4°C in a refrigerator.

Animals: Healthy male wistar rats (180-250 g) were obtained from the Animal House of the Obafemi Awolowo University, Ile-Ife, Nigeria. The animals were housed under normal laboratory conditions of humidity, temperature and light (12 h day, 12 h night). They were allowed free access to drinking water and animal pellete. The principle of Laboratory Animal Care (NIH Publication No.85-23) guidelines and procedure were used in the study (NIH, 1985).

Induction of diabetes mellitus: To induce diabetes in the experimental animals, they were given 120 mg kg⁻¹ body weight of alloxan monohydrate intraperitoneally as a single dose (Bavarva and Narasimhacharya, 2007). Eight days after the administration of alloxan, the fasting plasma glucose levels of the rats were measured by glucose oxidative method (Manzella *et al.*, 2001). Rats with plasma glucose level >140 mg dL⁻¹ were considered diabetic. The rats were divided into five groups of 5 rats per group.

Collection of blood samples: Blood sample drawn from the caudal vein of the rats were collected into heparinized specimen bottles before and 8 days after administration of alloxan. The final blood sample collection was done 24 h after the last dose of the extract of *Momordica charantia* fruit was administered. Blood samples were also taken from the normal (non-diabetic) rats before and after the administration of the extract for 28 days. The samples were then centrifuged at 3000 rpm for 10 min. The plasma samples obtained were stored in a refrigerator at 4°C and then used for the estimation of blood glucose level.

Experimental procedure: Five groups of diabetic rats and five groups of normal rats (5 rats/group) were used for the experiment. For both normal and diabetic groups, Group A which is the control, received distilled water ad libitum daily for 28 days. Group B, C and D received daily doses of 200, 400 and 600 mg kg⁻¹ of MCE respectively for 28 days. Group E was given 10 mg kg⁻¹ chlorpropamide daily for 28 days. All the drugs were administered orally. Blood samples were collected 24 h after the last dose and the fasting blood glucose level was measured using glucose oxidative method.

Statistical analysis: The SPSS software package was used for statistical analysis. Values obtained from the study were expressed as Mean and Standard Error of Mean (SEM). Statistical significance was determined by Student t-test. Values with p<0.05 were considered significant.

RESULTS

The methanol extract of *Momordica charantia* exhibited hypoglycemic effect in normal rats and anti-hyperglycemic effect in alloxan-diabetic rats. As shown in Table 1, there was a sharp increase in plasma glucose level of the rats after treatment with alloxan. This increase in glucose level was reversed after the administration of *Momordica charantia* extract. The results presented in Table 2 shows that 200 mg kg⁻¹ of the extract reduced blood glucose from 199.2±8.2 to 151.5±9.0. 400 mg kg⁻¹ MCE decreased blood glucose from 184.3±6.9 to 132.6±7.1 while 600 mg kg⁻¹ produced the highest anti-hyperglycemic effect, lowering blood glucose from 192.5±5.3 to 122.2±3.9. The effect of the extract in normal rats (non-diabetic) presented in Table 3 also

Table 1: Plasma glucose levels before and after induction of diabetes with alloxan

Group (n = 5)	Plasma glucose before induction (mg dL ⁻¹)	Plasma glucose after induction (mg dL ⁻¹)
A (Control)	114.2±5.9	188.4±6.5
B (200 mg kg ⁻¹ MCE)	101.0±34.7	199.2±8.2
C (400 mg kg ⁻¹ MCE)	108.0±27.5	184.3±6.9
D (600 mg kg ⁻¹ MCE)	99.4±6.3	192.5±5.3
E (10 mg kg ⁻¹ Chlorp)	118.3±7.7	209.3±9.9

Each value represents Mean±SEM

Table 2: Effect of MCE in alloxan diabetic rats

Group (n = 5)	Blood glucose before MCE (mg dL ⁻¹)	Blood glucose after MCE (mg dL ⁻¹)
A (Control)	188.4±6.5	218.2±9.8
B (200 mg kg ⁻¹ MCE)	199.2±8.2	151.5±9.0
C (400 mg kg ⁻¹ MCE)	184.3±6.9	132.6±7.1*
D (600 mg kg ⁻¹ MCE)	192.5±5.3	122.2±3.9*
E (10 mg kg ⁻¹ Chlorp)	209.3±9.9	119.4±4.6*

Each value represents Mean±SEM. *p<0.05 compared with control

Table 3: Effect of MCE in normal rats

Group (n = 5)	Blood glucose before MCE (mg dL ⁻¹)	Blood glucose after MCE (mg dL ⁻¹)
A (Control)	102.6±7.2	104.2±6.9
B (200 mg kg ⁻¹ MCE)	113.2±10.7	105.5±8.6
C (400 mg kg ⁻¹ MCE)	118.5±8.3	96.4±9.4*
D (600 mg kg ⁻¹ MCE)	122.1±12.4	91.9±7.0*
E (10 mg kg ⁻¹ Chlorp)	116.8±9.5	89.3±10.2*

Each value represents Mean±SEM. *p<0.05 compared with the control

showed a dose-dependent decrease in blood glucose levels. 200 mg kg⁻¹ MCE decreased blood glucose from 113.2±10.7 to 105.5±8.6. The 400 mg kg⁻¹ lowered blood glucose from 118.5±8.3 to 96.4±9.4 and 600 mg kg⁻¹ of the extract produced a reduction from 122.1±12.4 to 91.9±7.0. When compared with the control, the reductions in blood glucose by 400 and 600 mg kg⁻¹ of MCE in normal and diabetic rats were statistically significant (p<0.05).

DISCUSSION

From the result obtained in this study, *Momordica charantia* fruit methanol extract produced a dose-dependent decrease in blood glucose level of normal and alloxan diabetic rats. The observed reduction in blood glucose was statistically significant with the administration of 400 and 600 mg kg⁻¹ of the extract. The decrease in blood glucose produced by the extract at this dose range is also comparable to that produced by chlorpropamide, a standard hypoglycemic drug. A good number of earlier studies have reported the beneficial effects of bittergourd in diabetic animal models. For example, a study by Miura *et al.* (2001) showed that there was a significant reduction in blood glucose of diabetic animals after the administration of *Momordica charantia* fruit juice. Oral administration of *Momordica charantia* seed extract at a dose of 150 mg kg⁻¹ body weight to STZ-induced diabetic rats for a period of 30 days significantly restored the alterations in enzyme activity to near normal level (Sathishsekar and Rajasekaran, 2007). A mild hypoglycemic effect was observed with 250 mg kg⁻¹ of methanolic extract of *Momordica charantia* leaves in alloxan treated wistar rats. However, with 500 mg kg⁻¹ of the extract, a significant hypoglycemic effect was reported (Ataman *et al.*, 2006). Shetty *et al.* (2005) also observed an amelioration of about 30% in fasting blood glucose of diabetic rats fed with bittergourd. Present results corroborated these earlier reports. With 600 mg kg⁻¹ of the fruit extract, we observed a 36% decrease in blood glucose of diabetic rats and about 18% decrease in normal rats.

The mechanism by which *Momordica charantia* exerts its hypoglycemic effects is not yet fully understood. However, studies have shown that it has

some insulinomimetic effects. For instance, *Momordica charantia* fruit extract augmented glucose uptake and up-regulated Glu-4, a glucose transporter. These effects were comparable with those produced by insulin and rosiglitazone (Kumar *et al.*, 2009). *Momordica charantia* has also been shown to stimulate lipogenesis and inhibits hepatic glucogenetic enzymes on tissue preparation *in vitro* (Raman and Lau, 1996). Another possible mechanism of action is decreased intestinal absorption of glucose but this has not been experimentally established. Furthermore, a number of phytochemicals have been isolated from *Momordica charantia*. These include a polypeptide (p-insulin), a steroid (charantin) and a pyrimidine nucleoside (vicine). These are suspected to be the hypoglycemic components of the plant (Rao *et al.*, 2001).

Further investigations therefore need to be carried out on the plant to isolate the actual hypoglycemic agents and to elucidate the chemical structures of these components. More study also need to be done to establish the mechanism by which the plant exerts its anti-diabetic effects.

In conclusion, this study showed that *Momordica charantia* fruit possesses hypoglycemic properties and it may be a good alternative in the treatment of diabetes mellitus

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